WHAT IS CLAIMED IS:

1. A diagnostic agent comprising a diagnostic metal and a compound, wherein the compound comprises:

i) 1-10 targeting moieties;

ii) a chelator; and

iii) 0-1 linking groups between the targeting moiety and chelator;

wherein the targeting moiety is a matrix metalloproteinase inhibitor; and

wherein the chelator is capable of conjugating to the diagnostic metal.

2. A diagnostic agent according to claim 1, wherein the targeting moiety is a matrix metalloproteinase inhibitor having an inhibitory constant K_i of <1000 nM.

3. A diagnostic agent according to claim 1, wherein the targeting moiety is a matrix metalloproteinase inhibitor having an inhibitory constant K_i of <100 nM.

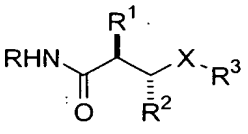
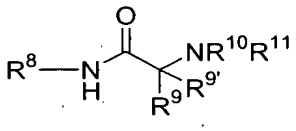
4. A diagnostic agent according to claim 1, comprising 1-5 targeting moieties.

5. A diagnostic agent according to claim 1, comprising one targeting moiety.

6. A diagnostic agent of claim 1, wherein the targeting moiety is an inhibitor of one or more matrix metalloproteinases selected from the group consisting of MMP-1, MMP-2, MMP-3, MMP-9, and MMP-14.

7. A diagnostic agent of claim 6, wherein the targeting moiety is an inhibitor of one or more matrix metalloproteinases selected from the group consisting of MMP-2, MMP-9, and MMP-14.

8. A diagnostic agent according to claim 1 wherein the targeting moiety is a matrix metalloproteinase inhibitor of the formulae (Ia) or (Ib):

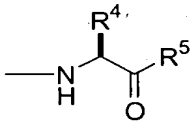

, or

; wherein,

R is independently OH or $-CH_2SH$;

R^1 is independently selected at each occurrence from the group: H, OH, C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, and heterocycle-S-CH_2-;

R^2 is independently C_{1-20} alkyl;

X is independently C=O or SO_2, provided when X is C=O, R^3 is


, and when X is SO_2, R^3 is independently selected from the group: aryl substituted with 0-2 R^6, and heterocycle substituted with 0-2 R^6;

R^4 is independently selected at each occurrence from the group: C_{1-6} alkyl, phenyl, and benzyl;

R^5 is independently at each occurrence from the group: NH(C_{1-6} alkyl), NH-phenyl, and NH-heterocycle; wherein said alkyl, phenyl and heterocycle groups are optionally substituted with a bond to the linking group or a bond to the chelator;

R^6 is independently aryloxy substituted with 0-3 R^7;

R^7 is independently halogen or methoxy;

or alternatively,

R^1 and R^4 may be taken together to form a bridging group of the formula $-(CH_2)_3$-O-phenyl-CH_2-, optionally substituted with a bond to the linking group or a bond to the chelator;

or alternatively,

R^1 and R^2 may be taken together to form a bridging group of the formula $-(CH_2)_3$-NH-, optionally substituted with a bond to the linking group or a bond to the chelator; or

R^1 and R^2 taken together with the nitrogen and carbon atom through which they are attached form a C_{5-7} atom saturated ring system substituted with one or more substituents selected from the group consisting of: a bond to Ln, a bond to Ch, and $-C(=O)-NR^{29}R^{30}$;

R^8 is independently at each occurrence OH or phenyl, optionally substituted with a bond to the linking group or a bond to the chelator, provided that when R^8 is phenyl, R^{10} is $-C(=O)-CR^{12}-NH-CH(CH_3)-COOH$;

R^9 and $R^{9'}$ are independently H, C_{1-6} alkyl optionally substituted with a bond to the linking group or a bond to the chelator, or are taken together with the carbon atom to which R^9 and $R^{9'}$ are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system substituted with R^6 and optionally substituted with a bond to the linking group or a bond to the chelator;

R^{10} and R^{11} are independently H, or C_{1-6} alkyl optionally substituted with a bond to the linking group or a bond to the chelator, or are taken together with the nitrogen atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted with 0-3 R^{27}, a bond to the linking group or a bond to the chelator;

or alternatively,

R^9 and R^{10} are taken together with the carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted with a bond to the linking group or a bond to the chelator; and

R^{12} is independently C_{1-20} alkyl;

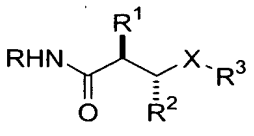
R^{27} is =O, C1-4 alkyl, or phenyl substituted with R^{28};

R^{28} is a phenoxy group substituted with 0-2 OCH_3 groups;

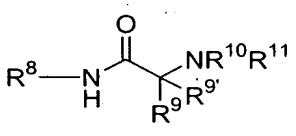
R^{29} and R^{30} taken together with the nitrogen atom through which they are attached form a C5-7 atom saturated ring system substituted with R^{31}; and

R^{31} is a benzyloxy group substituted with C1-4 alkyl.

9. A diagnostic agent according to claim 8 wherein the targeting moiety is a matrix metalloproteinase inhibitor of the formulae (Ia) or (Ib):



, or



; wherein,

R is OH;

R^1 is independently selected at each occurrence from the group: H, OH, C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, and heterocycle-S-CH_2-;

R^2 is independently C_{1-6} alkyl;

X is C=O;

R^4 is independently selected at each occurrence from the group: C_{1-6} alkyl, phenyl, and benzyl;

R^5 is independently at each occurrence from the group: NH(C_{1-6} alkyl), NH-phenyl, and NH-heterocycle; wherein said alkyl, phenyl and heterocycle groups are optionally substituted with a bond to the linking group or a bond to the chelator;

R^6 is independently aryloxy substituted with 0-3 R^7;

R^7 is independently halogen or methoxy;

or alternatively,

R^1 and R^4 may be taken together to form a bridging group of the formula -$(CH_2)_3$-O-phenyl-CH_2-, optionally substituted with a bond to the linking group or a bond to the chelator;

or alternatively,

R^1 and R^2 may be taken together to form a bridging group of the formula -$(CH_2)_3$-NH-, optionally substituted with a bond to the linking group or a bond to the chelator; or

R^1 and R^2 taken together with the nitrogen and carbon atom through which they are attached form a C_{5-7} atom saturated ring system substituted with one or more substituents selected from the group consisting of: a bond to Ln, a bond to Ch, and $-C(=O)-NR^{29}R^{30}$;

R^8 is OH;

R^9 and $R^{9'}$ are independently H, C_{1-6} alkyl optionally substituted with a bond to the linking group or a bond to the chelator, or are taken together with the carbon atom to which R^9 and $R^{9'}$ are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-1 heteroatoms selected from O, N, , said ring system optionally substituted with a bond to the linking group or a bond to the chelator;

R^{10} and R^{11} are independently H, or C_{1-6} alkyl optionally substituted with a bond to the linking group or a bond to the chelator, or are taken together with the nitrogen atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-1 heteroatoms selected from O, N, , said ring system optionally substituted with 0-3 R^{27}, a bond to the linking group or a bond to the chelator;

or alternatively,

R^9 and R^{10} are taken together with the carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-1 heteroatoms selected from O, N, , said ring system

optionally substituted with a bond to the linking group or a bond to the chelator; and

R^{12} is independently C_{1-6} alkyl;

R^{27} is =O, C1-4 alkyl, or phenyl substituted with R^{28};

R^{28} is a phenoxy group substituted with 0-2 OCH_3 groups;

R^{29} and R^{30} taken together with the nitrogen atom through which they are attached form a C5-7 atom saturated ring system substituted with R^{31}; and

R^{31} is a benzyloxy group substituted with C1-4 alkyl.

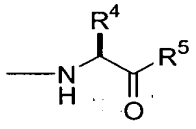
10. A diagnostic agent according to claim 8 wherein the targeting moiety is a matrix metalloproteinase inhibitor of the formulae (Ia) or (Ib):

wherein:

R is -OH;

R^2 is C_{1-6} alkyl;

X is C=O;

R^3 is  ;

R^1 and R^4 are taken together to form a bridging group of formula $-(CH_2)_3$-O-phenyl-CH_2-;

R^5 is NH(C1-6alkyl), substituted with a bond to the linking group or a bond to the chelator.

11. A diagnostic agent according to claim 8, wherein:

R is -OH;

R^9 is C_1 alkyl substituted with a bond to Ln;

R^{10} and R^{11} taken together with the nitrogen atom to which they are attached form a 5 atom saturated ring system, said right system is substituted with 0-3 R^{27};

R^{27} is =O, C1-4 alkyl, or phenyl substituted with R^{28}; and

R^{28} is a phenoxy group substituted with 0-2 OCH_3 groups.

12. A diagnostic agent according to claim 8 wherein the R is -OH;

R^1 and R^2 taken together with the nitrogen and carbon atom through which they are attached form a C_{5-7} atom saturated ring system substituted with one or more substituents selected from the group consisting of: a bond to Ln, a bond to Ch, and $-C(=O)-NR^{29}R^{30}$;

R^{29} and R^{30} taken together with the nitrogen atom through which they are attached form a C5-7 atom saturated ring system substituted with R^{31}; and

R^{31} is a benzyloxy group substituted with C1-4 alkyl.

13. A diagnostic agent according to claim 1 wherein the linking group is of the formula:

$((W^1)_h-(CR^{13}R^{14})_g)_x-(Z)_k-((CR^{13a}R^{14a})_{g'}-(W^2)_{h'})_{x'}$;

W^1 and W^2 are independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, $NR^{15}C(=O)$, $C(=O)NR^{15}$, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO_2, SO_2NH, $-(OCH_2CH_2)_{76-84}$, $(OCH_2CH_2)_s$, $(CH_2CH_2O)_{s'}$, $(OCH_2CH_2CH_2)_{s''}$, $(CH_2CH_2CH_2O)_t$, and $(aa)_{t'}$;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R^{16}, C_{3-10} cycloalkyl substituted with 0-3 R^{16}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{16};

R^{13}, R^{13a}, R^{14}, R^{14a}, and R^{15} are independently selected at each occurrence from the group: H, =O, COOH, SO_3H, PO_3H, C_1-C_5 alkyl substituted with 0-3 R^{16}, aryl substituted with 0-3 R^{16}, benzyl substituted with 0-3 R^{16}, and C_1-C_5 alkoxy substituted with 0-3 R^{16}, $NHC(=O)R^{17}$, $C(=O)NHR^{17}$, $NHC(=O)NHR^{17}$, NHR^{17}, R^{17}, and a bond to the chelator;

R^{16} is independently selected at each occurrence from the group: a bond to the chelator, $COOR^{17}$, $C(=O)NHR^{17}$, $NHC(=O)R^{17}$, OH, NHR^{17}, SO_3H, PO_3H, $-OPO_3H_2$, $-OSO_3H$, aryl substituted with 0-3 R^{17}, C_{1-5} alkyl substituted with 0-1 R^{18}, C_{1-5} alkoxy substituted with 0-1 R^{18}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{17};

R^{17} is independently selected at each occurrence from the group: H, alkyl substituted with 0-1 R^{18}, aryl substituted with 0-1 R^{18}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{18}, C_{3-10} cycloalkyl substituted with 0-1 R^{18}, polyalkylene glycol substituted with 0-1 R^{18}, carbohydrate substituted with 0-1 R^{18}, cyclodextrin substituted with 0-1 R^{18}, amino acid substituted with 0-1 R^{18}, polycarboxyalkyl substituted with 0-1 R^{18}, polyazaalkyl substituted with 0-1 R^{18}, peptide substituted with 0-1 R^{18}, wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to the chelator;

R^{18} is a bond to the chelator;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;
h' is selected from 0, 1, and 2;
g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s" is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
x is selected from 0, 1, 2, 3, 4, and 5; and
x' is selected from 0, 1, 2, 3, 4, and 5.

14. A diagnostic agent according to claim 13 wherein

W^1 and W^2 are independently selected at each occurrence from the group: O, NH, NHC(=O), C(=O)NH, $NR^{15}C(=O)$, $C(=O)NR^{15}$, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO_2, $-(CH_2CH_2O)_{76-84}-$, $(OCH_2CH_2)_s$, $(CH_2CH_2O)_{s'}$, $(OCH_2CH_2CH_2)_{s"}$, $(CH_2CH_2CH_2O)_t$, and $(aa)_{t'}$;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-1 R^{16}, C_{3-10} cycloalkyl substituted with 0-1 R^{16}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{16};

R^{13}, R^{13a}, R^{14}, R^{14a}, and R^{15} are independently selected at each occurrence from the group: H, =O, COOH, SO_3H, C_1-C_5 alkyl substituted with 0-1 R^{16}, aryl substituted with 0-1 R^{16}, benzyl substituted with 0-1 R^{16}, and C_1-C_5 alkoxy substituted with 0-1 R^{16}, $NHC(=O)R^{17}$, $C(=O)NHR^{17}$, $NHC(=O)NHR^{17}$, NHR^{17}, R^{17}, and a bond to the chelator;

k is 0 or 1;
s is selected from 0, 1, 2, 3, 4, and 5;
s' is selected from 0, 1, 2, 3, 4, and 5;
s" is selected from 0, 1, 2, 3, 4, and 5; and
t is selected from 0, 1, 2, 3, 4, and 5.

15 A diagnostic agent according to claim 13 wherein wherein:
W^1 is $C(=O)NR^{15}$;
h is 1;
g is 3;
R^{13} and R^{14} are independently H;
x is 1;
k is 0;
g'is 0;
h' is 1;
W^2 is NH; and
x' is 1.

16. A diagnostic agent according to claim 13 wherein
x is 0;
k is 1;
Z is aryl substituted with 0-3 R^{16};
g' is 1;
W^2 is NH;
R^{13a} and R^{14a} are independently H;
h' is 1; and
x' is 1.

17. A diagnostic agent according to claim 13 wherein
W^1 is $C(=O)NR^{15}$;
h is 1;
g is 2;
R^{13} and R^{14} are independently H;
x is 1;

k is 0;
g' is 1;
R^{13a} and R^{14a} are independently H; or C1-5 alkyl substituted with 0-3 R^{16};
R^{16} is SO_3H;
W^2 is NHC(=O) or NH;
h' is 1; and
x' is 2.

18. A diagnostic agent according to claim 13 wherein
W^1 is C(=O)NH;
h is 1;
g is 3;
R^{13} and R^{14} are independently H;
k is 0;
g' is 0;
x is 1;
W^2 is -NH(C=O)- or $-(OCH_2CH_2)_{76-84}-$;
h' is 2; and
x' is 1.

19. A diagnostic agent according to claim 13 wherein
x is 0;
k is 0;
g' is 3;
h' is 1;
W^2 is NH; and
x' is 1.

20. A diagnostic agent according to claim 13 wherein
x is 0;
Z is aryl substituted with 0-3 R^{16};
k is 1;
g' is 1;

$R^{13a}R^{14a}$ are independently H;

W^2 is NHC(=O) or $-(OCH2CH2)_{76-84}-$; and

x' is 1.

21. A diagnostic agent according to claim 13 wherein

W^1 is C=O;

g is 2;

R^{13} and R^{14} are independently H;

k is 0;

g'is 0;

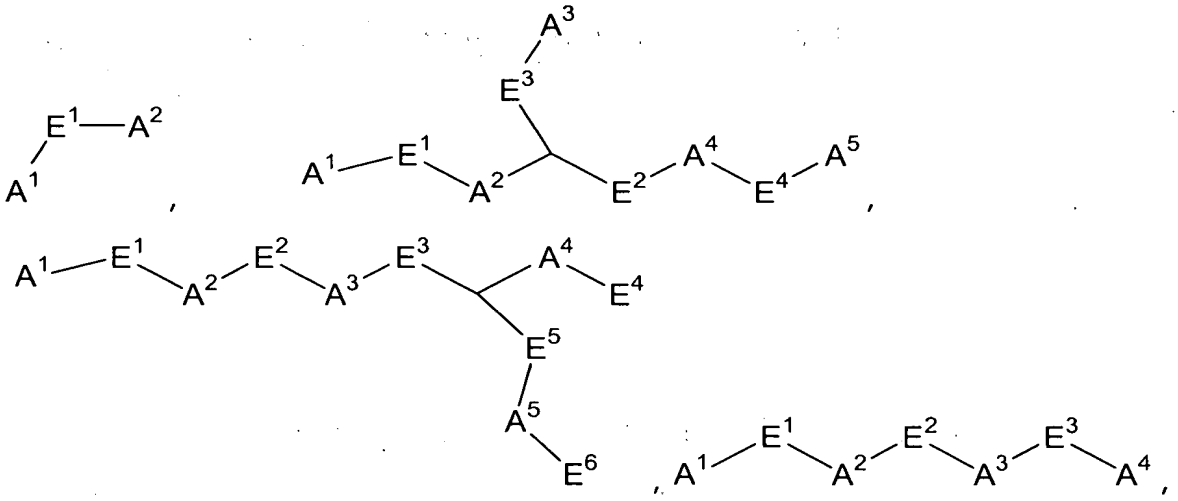
h' is 1;

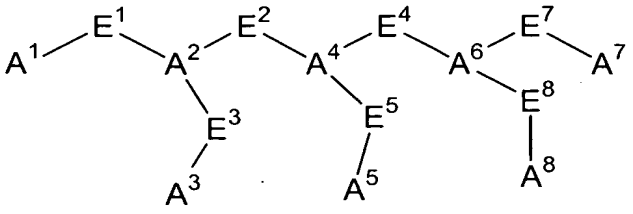
W^2 is NH; and

x' is 1.

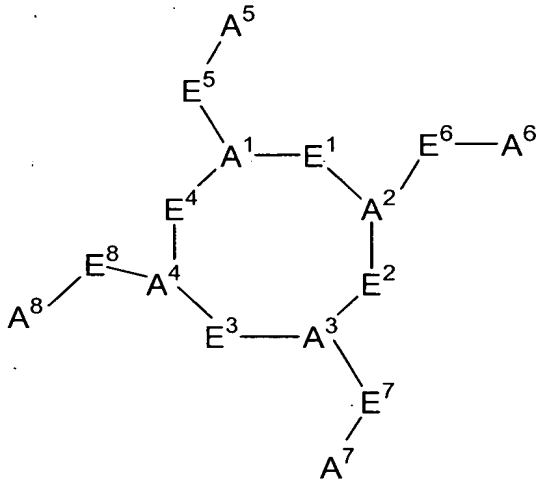
22. A compound according to claim 1 wherein the linking group is absent.

23. A diagnostic agent according to claim 1 wherein the chelator is a metal bonding unit having a formula selected from the group:





, and



;

A^1, A^2, A^3, A^4, A^5, A^6, A^7, and A^8 are independently selected at each occurrence from the group: N, NR^{26}, NR^{19}, $NR^{19}R^{20}$, S, SH, -S(Pg), O, OH, PR^{19}, $PR^{19}R^{20}$, -O-P(O)(R^{21})-O-, $P(O)R^{21}R^{22}$, a bond to the targeting moiety and a bond to the linking group;

Pg is a thiol protecting group;

E^1, E^2, E^3, E^4, E^5, E^6, E^7, and E^8 are independently a bond, CH, or a spacer group independently selected at each occurrence from the group: C_1-C_{16} alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, C_{3-10} cycloalkyl substituted with 0-3 R^{23}, heterocyclo-C_{1-10} alkyl substituted with 0-3 R^{23}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10} aryl-C_{1-10} alkyl substituted with 0-3 R^{23}, C_{1-10} alkyl-C_{6-10} aryl-substituted with 0-3 R^{23}, and a 5-10 membered heterocyclic

ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23};

R^{19} and R^{20} are each independently selected from the group: a bond to the linking group, a bond to the targeting moiety, hydrogen, C_1-C_{10} alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, C_{1-10} cycloalkyl substituted with 0-3 R^{23}, heterocyclo-C_{1-10} alkyl substituted with 0-3 R^{23}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10} aryl-C_{1-10} alkyl substituted with 0-3 R^{23}, C_{1-10} alkyl-C_{6-10} aryl-substituted with 0-3 R^{23}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23}, and an electron, provided that when one of R^{19} or R^{20} is an electron, then the other is also an electron;

R^{21} and R^{22} are each independently selected from the group: a bond to the linking group, a bond to the targeting moiety, -OH, C_1-C_{10} alkyl substituted with 0-3 R^{23}, C_1-C_{10} alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, C_{3-10} cycloalkyl substituted with 0-3 R^{23}, heterocyclo-C_{1-10} alkyl substituted with 0-3 R^{23}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10} aryl-C_{1-10} alkyl substituted with 0-3 R^{23}, C_{1-10} alkyl-C_{6-10} aryl- substituted with 0-3 R^{23}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23};

R^{23} is independently selected at each occurrence from the group: a bond to the linking group, a bond to the targeting moiety, =O, F, Cl, Br, I, $-CF_3$, -CN, $-CO_2R^{24}$, $-C(=O)R^{24}$, $-C(=O)N(R^{24})_2$, -CHO, $-CH_2OR^{24}$, $-OC(=O)R^{24}$, $-OC(=O)OR^{24a}$, $-OR^{24}$, $-OC(=O)N(R^{24})_2$, $-NR^{25}C(=O)R^{24}$, $-NR^{25}C(=O)OR^{24a}$, $-NR^{25}C(=O)N(R^{24})_2$, $-NR^{25}SO_2N(R^{24})_2$, $-NR^{25}SO_2R^{24a}$, $-SO_3H$, $-SO_2R^{24a}$, $-SR^{24}$, $-S(=O)R^{24a}$, $-SO_2N(R^{24})_2$, $-N(R^{24})_2$, $-NHC(=S)NHR^{24}$, $=NOR^{24}$, NO_2, $-C(=O)NHOR^{24}$, $-C(=O)NHNR^{24}R^{24a}$, $-OCH_2CO_2H$, 2-(1-morpholino)ethoxy, C_1-C_5 alkyl, C_2-C_4 alkenyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkylmethyl, C_2-C_6 alkoxyalkyl, aryl substituted with 0-2 R^{24}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O; and

wherein at least one of A^1, A^2, A^3, A^4, A^5, A^6, A^7, A^8 or R^{23} is a bond to the linking group or targeting moiety;

R^{24}, R^{24a}, and R^{25} are independently selected at each occurrence from the group: a bond to the linking group, a bond to the targeting moiety, H, C_1-C_6 alkyl, phenyl, benzyl, C_1-C_6 alkoxy, halide, nitro, cyano, and trifluoromethyl; and

R^{26} is a co-ordinate bond to a metal or a hydrazine protecting group; or a pharmaceutically acceptable salt thereof.

24. A diagnostic agent according to claim 23 wherein:

A^1, A^2, A^3, A^4, A^5, A^6, A^7, and A^8 are independently selected at each occurrence from the group: NR^{19}, $NR^{19}R^{20}$, S, SH, OH, a bond to the targeting moiety and a bond to the linking group;

E^1, E^2, E^3, E^4, E^5, E^6, E^7, and E^8 are independently a bond, CH, or a spacer group independently selected at each occurrence from the group: C_1-C_{10} alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, C_{3-10} cycloalkyl

substituted with 0-3 R^{23}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23};

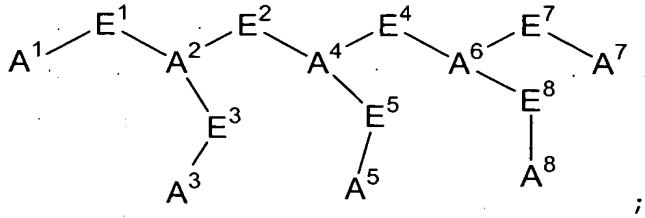
wherein at least one of A^1, A^2, A^3, A^4, A^5, A^6, A^7, A^8 and R^{23} is a bond to the linking group or the targeting moiety;

R^{19}, and R^{20} are each independently selected from the group: a bond to the targeting moiety, a bond to the linking group, hydrogen, C_1-C_{10} alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23}, and an electron, provided that when one of R^{19} or R^{20} is an electron, then the other is also an electron;

R^{23} is independently selected at each occurrence from the group: a bond to the targeting moiety, a bond to the linking group, =O, F, Cl, Br, I, $-CF_3$, -CN, $-CO_2R^{24}$, $-C(=O)R^{24}$, $-C(=O)N(R^{24})_2$, $-CH_2OR^{24}$, $-OC(=O)R^{24}$, $-OC(=O)OR^{24a}$, $-OR^{24}$, $-OC(=O)N(R^{24})_2$, $-NR^{25}C(=O)R^{24}$, $-NR^{25}C(=O)OR^{24a}$, $-NR^{25}C(=O)N(R^{24})_2$, $-NR^{25}SO_2N(R^{24})_2$, $-NR^{25}SO_2R^{24a}$, $-SO_3H$, $-SO_2R^{24a}$, $-S(=O)R^{24a}$, $-SO_2N(R^{24})_2$, $-N(R^{24})_2$, $-NHC(=S)NHR^{24}$, $=NOR^{18}$, $-C(=O)NHNR^{18}R^{18a}$, $-OCH_2CO_2H$, and 2-(1-morpholino)ethoxy; and

R^{24}, R^{24a}, and R^{25} are independently selected at each occurrence from the group: a bond to the linking group, H, and C_1-C_6 alkyl.

25. A diagnostic agent according to claim 23 wherein the chelator is of the formula:



;

A^1 is a bond to the linking group;

A^2, A^4, and A^6 are each N;

A^3, A^5, A^7 and A^8 are each OH;

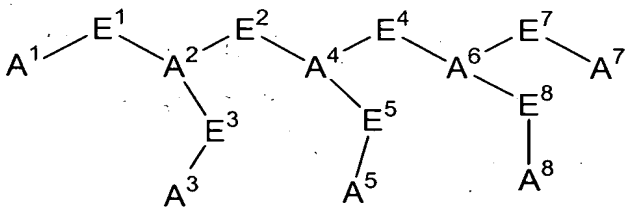
E^1, E^2, and E^4 are C2 alkyl;

E^3, E^5, E^7, and E^8 are C_2 alkyl substituted with 0-1 R^{23};

R^{23} is =O.

26. A diagnostic agent according to claim 23 wherein the chelator is of the formula:

Ch is



;

wherein:

A5 is a bond to Ln;

A^1, A^3, A^7 and A^8 are each OH;

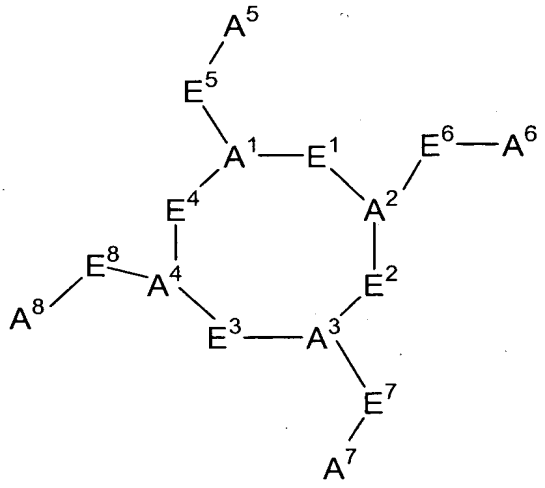
A^2, A^4 and A^6 are each NH;

E^1, E^3, E^5, E^7, and E^8 are C_2 alkyl substituted with 0-1 R^{23};

E^2, and E^4, are C_2 alkyl;

R^{23} is =O.

27. A diagnostic agent according to claim 23 wherein the chelator is of the formula:



;

A^1, A^2, A^3 and A^4 are each N;

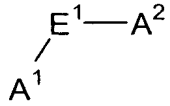
A^5, A^6 and A^8 are each OH;

A^7 is a bond to L_n;

E^1, E^2, E^3, E^4 are each independently C_2 alkyl; and

E^5, E^6, E^7, E^8 are each independently C_2 alkyl substituted with 0-1 R^{23};

R^{23} is =O.

28. A diagnostic agent according to claim 23 wherein the chelator is of the formula:  ;

A^1 is NR^{26};

R^{26} is a co-ordinate bond to a metal or a hydrazine protecting group;;

E^1 is a bond;

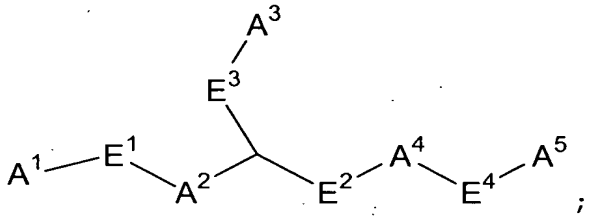
A^2 is NHR^{19};

R^{19} is a heterocycle substituted with R^{23}, the heterocycle being selected from pyridine and pyrimidine;

R^{23} is selected from a bond to the linking group, $C(=O)NHR^{24}$ and $C(=O)R^{24}$; and

R^{24} is a bond to the linking group.

29. A diagnostic agent according to claim 23 wherein the chelator is of the formula:



;

wherein:

A^1 and A^5 are each $-S(Pg)$;

Pg is a thiol protecting group;

E^1 and E^4 are C_2 alkyl substituted with 0-1 R^{23};

R^{23} is $=O$;

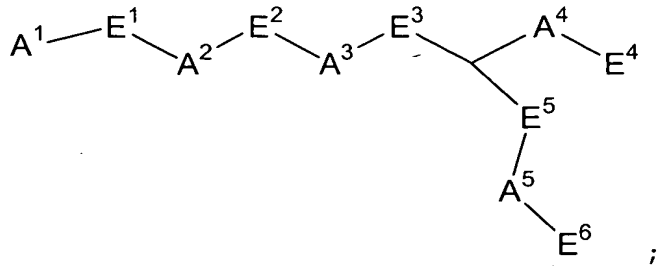
A^2 and A^4 are each $-NH$;

E^2 is CH_2;

E^3 is C_{1-3} alkyl substituted with 0-1 R^{23};

A^3 is a bond to Ln.

30. A diagnostic agent according to claim 23 wherein the chelator is of the formula:



;

wherein:

A^1 is a bond to Ln;

E^1 is C_1 alkyl substituted by R^{23};

A^2 is NH;

E^2 is C_2 alkyl substituted with 0-1R^{23};

A^3 is -O-P(O)(R^{21})-O;

E^3 is C_1 alkyl;

A^4 and A^5 are each -O-;

E^4 and E^6 are each independently C_{1-16} alkyl substituted with 0-1R^{23};

E^5 is C_1 alkyl;

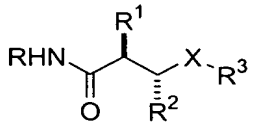
R^{21} is -OH; and

R^{23} is =O.

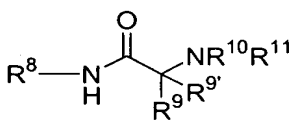
31. A diagnostic agent according to claim 1 having the formula:

$$(Q)_d\text{-}L_n\text{-}C_h$$

wherein, Q is a compound of Formulae (Ia) or (Ib):



, or



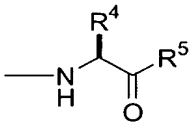
; wherein,

R is independently OH or $-CH_2SH$;

R^1 is independently selected at each occurrence from the group: H, OH, C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, and heterocycle-S-CH_2-;

R^2 is independently C_{1-20} alkyl;

X is independently C=O or SO_2, provided when X is C=O, R^3 is



, and when X is SO_2, R^3 is independently selected from the group: aryl substituted with 0-2 R^6, and heterocycle substituted with 0-2 R^6;

R^4 is independently selected at each occurrence from the group: C_{1-6} alkyl, phenyl, and benzyl;

R^5 is independently at each occurrence from the group: NH(C_{1-6} alkyl), NH-phenyl, and NH-heterocycle; wherein said alkyl, phenyl and heterocycle groups are optionally substituted with a bond to L_n;

R^6 is independently aryloxy substituted with 0-3 R^7;

R^7 is independently halogen or methoxy;

or alternatively,

R^1 and R^4 may be taken together to form a bridging group of the formula $-(CH_2)_3$-O-phenyl-CH_2-, optionally substituted with a bond to L_n;

or alternatively,

R^1 and R^2 may be taken together to form a bridging group of the formula $-(CH_2)_3$-NH-, optionally substituted with a bond to L_n; or

R^1 and R^2 taken together with the nitrogen and carbon atom through which they are attached form a C_{5-7} atom saturated ring system substituted with one or more substituents selected from the group consisting of: a bond to Ln, a bond to Ch, and $-C(=O)-NR^{29}R^{30}$;

R^8 is independently at each occurrence OH or phenyl, optionally substituted with a bond to L_n, provided that when R^8 is phenyl, R^{10} is $-C(=O)-CR^{12}-NH-CH(CH_3)-COOH$;

R^9 and $R^{9'}$ are independently H, C_{1-6} alkyl optionally substituted with a bond to L_n, or are taken together with the carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system substituted with R^6 and optionally substituted with a bond to L_n;

R^{10} and R^{11} are independently H, or C_{1-6} alkyl optionally substituted with a bond to L_n, or are taken together with the nitrogen atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted with 0-3 R^{27} or a bond to L_n;

or alternatively,

R^9 and R^{10} are taken together with the carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted with a bond to L_n;

R^{12} is independently C_{1-20} alkyl;

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

L_n is a linking group having the formula:

$((W^1)_h\text{-}(CR^{13}R^{14})_g)_x\text{-}(Z)_k\text{-}((CR^{13a}R^{14a})_{g'}\text{-}(W^2)_{h'})_{x'}$;

W^1 and W^2 are independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, $NR^{15}C(=O)$, $C(=O)NR^{15}$, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO_2, SO_2NH, $-(OCH_2CH_2)_{76-84}$, $(OCH_2CH_2)_s$, $(CH_2CH_2O)_{s'}$, $(OCH_2CH_2CH_2)_{s''}$, $(CH_2CH_2CH_2O)_t$, and $(aa)_{t'}$;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R^{16}, C_{3-10} cycloalkyl substituted with 0-3 R^{16}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{16};

R^{13}, R^{13a}, R^{14}, R^{14a}, and R^{15} are independently selected at each occurrence from the group: H, =O, COOH, SO_3H, PO_3H, $C_1\text{-}C_5$ alkyl substituted with 0-3 R^{16}, aryl substituted with 0-3 R^{16}, benzyl substituted with 0-3 R^{16}, and $C_1\text{-}C_5$ alkoxy substituted with 0-3 R^{16}, $NHC(=O)R^{17}$, $C(=O)NHR^{17}$, $NHC(=O)NHR^{17}$, NHR^{17}, R^{17}, and a bond to C_h;

R^{16} is independently selected at each occurrence from the group: a bond to C_h, $COOR^{17}$, $C(=O)NHR^{17}$, $NHC(=O)R^{17}$, OH, NHR^{17}, SO_3H, PO_3H, $-OPO_3H_2$, $-OSO_3H$, aryl substituted with 0-3 R^{17},

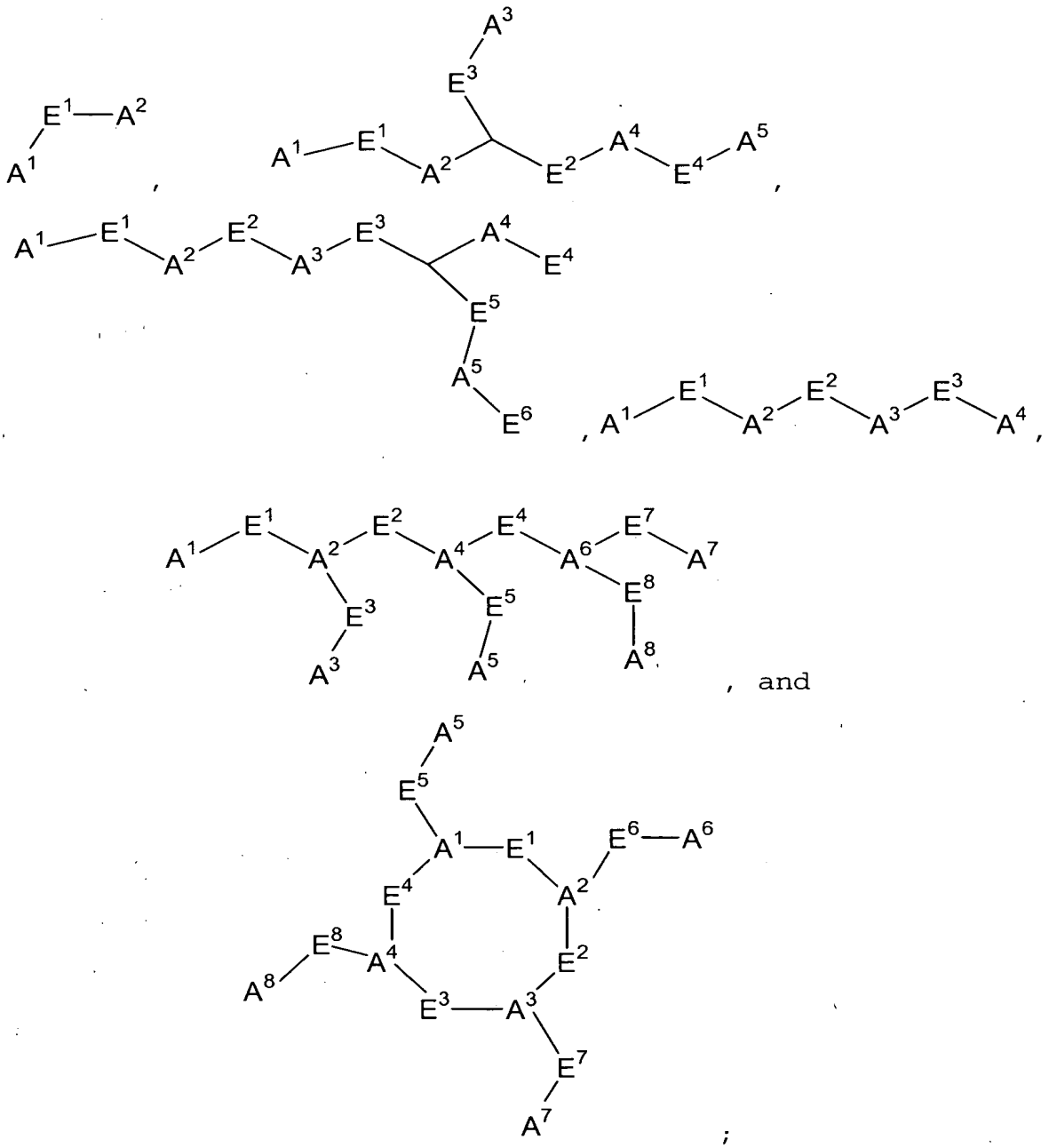
C_{1-5} alkyl substituted with 0-1 R^{18}, C_{1-5} alkoxy substituted with 0-1 R^{18}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{17};

R^{17} is independently selected at each occurrence from the group: H, alkyl substituted with 0-1 R^{18}, aryl substituted with 0-1 R^{18}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{18}, C_{3-10} cycloalkyl substituted with 0-1 R^{18}, polyalkylene glycol substituted with 0-1 R^{18}, carbohydrate substituted with 0-1 R^{18}, cyclodextrin substituted with 0-1 R^{18}, amino acid substituted with 0-1 R^{18}, polycarboxyalkyl substituted with 0-1 R^{18}, polyazaalkyl substituted with 0-1 R^{18}, peptide substituted with 0-1 R^{18}, wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to C_h;

R^{18} is a bond to C_h;

k is selected from 0, 1, and 2;
h is selected from 0, 1, and 2;
h' is selected from 0, 1, and 2;
g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s" is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
x is selected from 0, 1, 2, 3, 4, and 5;
x' is selected from 0, 1, 2, 3, 4, and 5;

C_h is a metal bonding unit having a formula selected from the group:



;

A^1, A^2, A^3, A^4, A^5, A^6, A^7, and A^8 are independently selected at each occurrence from the group: N, NR^{26}, NR^{19}, $NR^{19}R^{20}$, S, SH, -S(Pg), O, OH, PR^{19}, $PR^{19}R^{20}$, -O-P(O)(R^{21})-O-,

$P(O)R^{21}R^{22}$, a bond to the targeting moiety and a bond to the linking group;

Pg is a thiol protecting group;

E^1, E^2, E^3, E^4, E^5, E^6, E^7, and E^8 are independently a bond, CH, or a spacer group independently selected at each occurrence from the group: C_1-C_{16} alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, C_{3-10} cycloalkyl substituted with 0-3 R^{23}, heterocyclo-C_{1-10} alkyl substituted with 0-3 R^{23}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10} aryl-C_{1-10} alkyl substituted with 0-3 R^{23}, C_{1-10} alkyl-C_{6-10} aryl- substituted with 0-3 R^{23}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23};

R^{19} and R^{20} are each independently selected from the group: a bond to the linking group, a bond to the targeting moiety, hydrogen, C_1-C_{10} alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, C_{1-10} cycloalkyl substituted with 0-3 R^{23}, heterocyclo-C_{1-10} alkyl substituted with 0-3 R^{23}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10} aryl-C_{1-10} alkyl substituted with 0-3 R^{23}, C_{1-10} alkyl-C_{6-10} aryl- substituted with 0-3 R^{23}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23}, and an electron, provided that when one of R^{19} or R^{20} is an electron, then the other is also an electron;

R^{21} and R^{22} are each independently selected from the group: a bond to the linking group, a bond to the targeting moiety, -OH, C_1-C_{10} alkyl substituted with 0-3 R^{23}, C_1-C_{10} alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, C_{3-10} cycloalkyl substituted with 0-3 R^{23}, heterocyclo-C_{1-10} alkyl substituted with 0-3 R^{23}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10} aryl-C_{1-10} alkyl substituted with 0-3 R^{23}, C_{1-10} alkyl-C_{6-10} aryl- substituted with 0-3 R^{23}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23};

R^{23} is independently selected at each occurrence from the group: a bond to the linking group, a bond to the targeting moiety, =O, F, Cl, Br, I, $-CF_3$, -CN, $-CO_2R^{24}$, $-C(=O)R^{24}$, $-C(=O)N(R^{24})_2$, -CHO, $-CH_2OR^{24}$, $-OC(=O)R^{24}$, $-OC(=O)OR^{24a}$, $-OR^{24}$, $-OC(=O)N(R^{24})_2$, $-NR^{25}C(=O)R^{24}$, $-NR^{25}C(=O)OR^{24a}$, $-NR^{25}C(=O)N(R^{24})_2$, $-NR^{25}SO_2N(R^{24})_2$, $-NR^{25}SO_2R^{24a}$, $-SO_3H$, $-SO_2R^{24a}$, $-SR^{24}$, $-S(=O)R^{24a}$, $-SO_2N(R^{24})_2$, $-N(R^{24})_2$, $-NHC(=S)NHR^{24}$, $=NOR^{24}$, NO_2, $-C(=O)NHOR^{24}$, $-C(=O)NHNR^{24}R^{24a}$, $-OCH_2CO_2H$, 2-(1-morpholino)ethoxy, C_1-C_5 alkyl, C_2-C_4 alkenyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkylmethyl, C_2-C_6 alkoxyalkyl, aryl substituted with 0-2 R^{24}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O; and

wherein at least one of A^1, A^2, A^3, A^4, A^5, A^6, A^7, A^8 or R^{23} is a bond to the linking group or targeting moiety;

R^{24}, R^{24a}, and R^{25} are independently selected at each occurrence from the group: a bond to the linking group, a bond to the

targeting moiety, H, C_1-C_6 alkyl, phenyl, benzyl, C_1-C_6 alkoxy, halide, nitro, cyano, and trifluoromethyl; and

R^{26} is a co-ordinate bond to a metal or a hydrazine protecting group; or

a pharmaceutically acceptable salt thereof.

32. A diagnostic agent according to Claim 31, wherein:

h' is 1;

W^2 is NH; and

x' is 1.

33. A diagnostic agent according to Claim 31, wherein:

x is 0;

Z is aryl substituted with 0-3 R^{16};

k is 1;

g' is 1;

$R^{13a}R^{14a}$ are independently H;

W^2 is NHC(=O) or $-(OCH2CH2)_{76-84}-$; and

x' is 1.

34. A diagnostic agent according to Claim 31, wherein:

W^1 is C=O;

g is 2;

R^{13} and R^{14} are independently H;

k is 0;

g'is 0;

h' is 1;

W^2 is NH; and

x' is 1.

35. A diagnostic agent according to Claim 31, wherein:

2-{[5-(3-{2-[(6-Hydroxycarbamoyl-7-isobutyl-8-oxo-2-oxa-9-aza-bicyclo[10.2.2]hexadeca-1(15),12(16),13-triene-10-carbonyl)-

amino]-acetylamino}-propylcarbamoyl)-pyridin-2-yl]-hydrazonomethyl}-benzenesulfonic acid;

2-{[5-(4-{[(6-Hydroxycarbamoyl-7-isobutyl-8-oxo-2-oxa-9-aza-bicyclo[10.2.2]hexadeca-1(15),12(16),13-triene-10-carbonyl)-amino]-methyl}-benzylcarbamoyl)-pyridin-2-yl]-hydrazonomethyl}-benzenesulfonic acid;

2-[7-({N-[3-(2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}acetylamino)propyl]carbamoyl}methyl)-1,4,7,10-tetraaza-4,10-bis(carboxymethyl)cyclododecyl]acetic acid;

2-{7-[(N-{[4-({[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-carbonylamino}methyl)phenyl]methyl}carbamoyl)methyl]-1,4,7,10-tetraaza-4,10-bis(carboxymethyl)cyclododecyl}acetic acid;

2-(7-{[N-(1-{N-[3-(2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}acetylamino)propyl]carbamoyl}-2-sulfoethyl)carbamoyl]methyl}-1,4,7,10-tetraaza-4,10-bis(carboxymethyl)cyclododecyl)acetic acid;

2-[7-({N-[1-(N-{[4-({[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-carbonylamino}methyl)phenyl]methyl}carbamoyl)-2-sulfoethyl]carbamoyl}methyl)-1,4,7,10-tetraaza-4,10-bis(carboxymethyl)cyclododecyl]acetic acid;

2-({2-[({N-[3-(2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-

1(15),12(16),13-trien-3-yl]carbonylamino}acetylamino)propyl]carbamoyl}methyl)(carboxymethyl)amino}ethyl){2-[bis(carboxymethyl)amino]ethyl}amino]acetic acid;

2-[(2-{[(N-{[4-({[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-carbonylamino}methyl)phenyl]methyl}carbamoyl)methyl](carboxymethyl)amino}ethyl){2-[bis(carboxymethyl)amino]ethyl}amino]acetic acid;

N-[3-(2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}acetylamino)propyl]-4,5-bis[2-(ethoxyethylthio)acetylamino]pentanamide;

N-{[4-({[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}methyl)-phenyl]methyl}-4,5-bis[2-(ethoxyethylthio)acetylamino]-pentanamide;

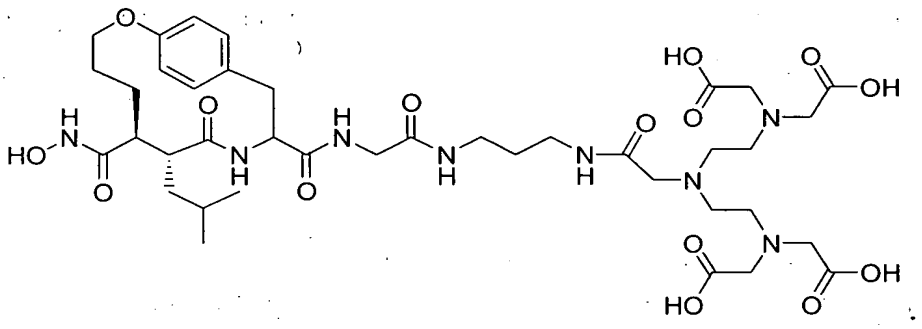
1-(1,2-Dipalmitoyl-sn-glycero-3-phosphoethanolamino)-α,ω-dicarbonylPEG$_{3400}$-2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}-N-(3-aminopropyl)acetamide;

1-(1,2-Dipalmitoyl-sn-glycero-3-phosphoethanolamino)-α,ω-dicarbonylPEG$_{3400}$-[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-N-{[4-(aminomethyl)phenyl]methyl}carboxamide conjugate;

2-[2-({5-[N-(5-(N-hydroxycarbamoyl)(5R)-5-{3-[4-(3,4-dimethoxyphenoxy)phenyl]-3-methyl-2-

oxopyrrolidinyl}pentyl)carbamoyl](2-pyridyl)}amino)(1Z)-2-azavinyl]benzenesulfonic acid;

2-(2-{[5-(N-{3-[3-(N-hydroxycarbamoyl)(4S)-4-({4-[(4-methylphenyl)methoxy]piperidyl}carbonyl)piperidyl]-3-oxopropyl}carbamoyl)(2-pyridyl)]amino}(1Z)-2-azavinyl)benzenesulfonic acid; and



36. A diagnostic agent according to claim 1 wherein the diagnostic metal is selected from the group consisting of: a paramagnetic metal, a ferromagnetic metal, a gamma-emitting radioisotope, or an x-ray absorber.

37. A diagnostic agent according to claim 36 wherein the diagnostic metal is radioisotope selected from the group consisting of ^{99m}Tc, ^{95}Tc, ^{111}In, ^{62}Cu, ^{64}Cu, ^{67}Ga, and ^{68}Ga.

38. A diagnostic agent according to claim 37 further comprising a first ancillary ligand and a second ancillary ligand capable of stabilizing the radioisotope.

39. A diagnostic agent according to Claim 37, wherein the radioisotope is ^{99m}Tc.

40. A diagnostic agent according to Claim 37, wherein the radioisotope is ^{111}In.

41. A diagnostic agent according to claim 36 wherein the paramagnetic metal ion is selected from the group consisting of Gd(III), Dy(III), Fe(III), and Mn(II).

42. A diagnostic agent according to claim 36 wherein the x-ray absorber is a metal is selected from the group consisting of: Re, Sm, Ho, Lu, Pm, Y, Bi, Pd, Gd, La, Au, Au, Yb, Dy, Cu, Rh, Ag, and Ir.

43. A diagnostic composition comprising a compound according to claim 1 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

44. A kit comprising a compound of Claim 1, or a pharmaceutically acceptable salt form thereof and a pharmaceutically acceptable carrier.

45. A kit according to Claim 44, wherein the kit further comprises one or more ancillary ligands and a reducing agent.

46. A kit according to Claim 45, wherein the ancillary ligands are tricine and TPPTS.

47 A kit according to Claim 45, wherein the reducing agent is tin(II).

48. A diagnostic agent comprising an echogenic gas and a compound, wherein the compound comprises:

i) 1-10 targeting moieties;

ii) a surfactant (Sf); and

iii) 0-1 linking groups between the targeting moiety and surfactant;

wherein the targeting moiety is a matrix metalloproteinase inhibitor; and

wherein the surfactant is capable of forming an echogenic gas filled lipid sphere or microbubble.

49. A diagnostic agent according to claim 48, wherein the targeting moiety is a matrix metalloproteinase inhibitor having an inhibitory constant K_i of <1000 nM.

50. A diagnostic agent according to claim 48, wherein the targeting moiety is a matrix metalloproteinase inhibitor having an inhibitory constant K_i of <100 nM.

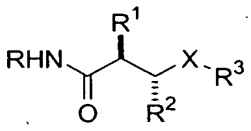
51. A diagnostic agent according to claim 48, comprising 1-5 targeting moieties.

52. A diagnostic agent according to claim 48, comprising one targeting moiety.

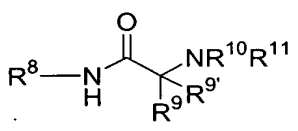
53. A diagnostic agent according to claim 48, wherein the targeting moiety is an inhibitor of one or more matrix metalloproteinases selected from the group consisting of MMP-1, MMP-2, MMP-3, MMP-9, and MMP-14.

54. A diagnostic agent according to claim 48, wherein the targeting moiety is an inhibitor of one or more matrix metalloproteinases selected from the group consisting of MMP-2, MMP-9, and MMP-14.

55. A diagnostic agent according to claim 48, wherein the targeting moiety is of the formulae (Ia) or (Ib):



, or



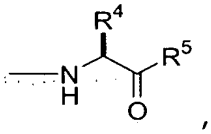
; wherein,

R is independently OH or $-CH_2SH$;

R^1 is independently selected at each occurrence from the group: H, OH, C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, and heterocycle-S-CH_2-;

R^2 is independently C_{1-20} alkyl;

X is independently C=O or SO_2, provided when X is C=O, R^3 is



, and when X is SO_2, R^3 is independently selected from the group: aryl substituted with 0-2 R^6, and heterocycle substituted with 0-2 R^6;

R^4 is independently selected at each occurrence from the group: C_{1-6} alkyl, phenyl, and benzyl;

R^5 is independently at each occurrence from the group: NH(C_{1-6} alkyl), NH-phenyl, and NH-heterocycle; wherein said alkyl, phenyl and heterocycle groups are optionally substituted with a bond to the linking group or a bond to the surfactant;

R^6 is independently aryloxy substituted with 0-3 R^7;

R^7 is independently halogen or methoxy;

or alternatively,

R^1 and R^4 may be taken together to form a bridging group of the formula -$(CH_2)_3$-O-phenyl-CH_2-, optionally substituted with a bond to the linking group or a bond to the surfactant;

or alternatively,

R^1 and R^2 may be taken together to form a bridging group of the formula $-(CH_2)_3-NH-$, optionally substituted with a bond to the linking group or a bond to the surfactant; or

R^1 and R^2 taken together with the nitrogen and carbon atom through which they are attached form a C_{5-7} atom saturated ring system substituted with one or more substituents selected from the group consisting of: a bond to Ln, a bond to Sf, and $-C(=O)-NR^{29}R^{30}$;

R^8 is independently at each occurrence OH or phenyl, optionally substituted with a bond to the linking group or a bond to the surfactant, provided that when R^8 is phenyl, R^{10} is $-C(=O)-CR^{12}-NH-CH(CH_3)-COOH$;

R^9 and $R^{9'}$ are independently H, C_{1-6} alkyl optionally substituted with a bond to the linking group or a bond to the surfactant, or are taken together with the carbon atom to which R^9 and $R^{9'}$ are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system substituted with R^6 and optionally substituted with a bond to the linking group or a bond to the surfactant;

R^{10} and R^{11} are independently H, or C_{1-6} alkyl optionally substituted with a bond to the linking group or a bond to the surfactant, or are taken together with the nitrogen atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted with 0-3 R^{27}, a bond to the linking group or a bond to the surfactant;

or alternatively,

R^9 and R^{10} are taken together with the carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted with a bond to the linking group or a bond to the surfactant; and

R^{12} is independently C_{1-20} alkyl;

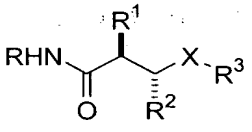
R^{27} is =O, C1-4 alkyl, or phenyl substituted with R^{28};

R^{28} is a phenoxy group substituted with 0-2 OCH_3 groups;

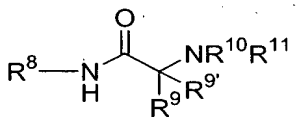
R^{29} and R^{30} taken together with the nitrogen atom through which they are attached form a C5-7 atom saturated ring system substituted with R^{31}; and

R^{31} is a benzyloxy group substituted with C1-4 alkyl.

56. A diagnostic agent according to claim 55 wherein wherein the targeting moiety is a matrix metalloproteinase inhibitor of the formulae (Ia) or (Ib):



, or



; wherein,

R is OH;

R^1 is independently selected at each occurrence from the group: H, OH, C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, and heterocycle-S-CH_2-;

R^2 is independently C_{1-6} alkyl;

X is C=O;

R^4 is independently selected at each occurrence from the group: C_{1-6} alkyl, phenyl, and benzyl;

R^5 is independently at each occurrence from the group: NH(C_{1-6} alkyl), NH-phenyl, and NH-heterocycle; wherein said alkyl, phenyl and heterocycle groups are optionally substituted with a bond to the linking group or a bond to the surfactant;

R^6 is independently aryloxy substituted with 0-3 R^7;

R^7 is independently halogen or methoxy;

or alternatively,

R^1 and R^4 may be taken together to form a bridging group of the formula $-(CH_2)_3$-O-phenyl-CH_2-, optionally substituted with a bond to the linking group or a bond to the surfactant;

or alternatively,

R^1 and R^2 may be taken together to form a bridging group of the formula $-(CH_2)_3$-NH-, optionally substituted with a bond to the linking group or a bond to the surfactant; or

R^1 and R^2 taken together with the nitrogen and carbon atom through which they are attached form a C_{5-7} atom saturated ring system substituted with one or more substituents selected from the group consisting of: a bond to Ln, a bond to Sf, and $-C(=O)-NR^{29}R^{30}$;

R^8 is OH;

R^9 and $R^{9'}$ are independently H, C_{1-6} alkyl optionally substituted with a bond to the linking group or a bond to the surfactant, or are taken together with the carbon atom to which R^9 and $R^{9'}$ are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-1 heteroatoms selected from O, N, , said ring system optionally substituted with a bond to the linking group or a bond to the surfactant;

R^{10} and R^{11} are independently H, or C_{1-6} alkyl optionally substituted with a bond to the linking group or a bond to the surfactant, or are taken together with the nitrogen atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-1 heteroatoms selected from O, N, , said ring system optionally substituted with 0-3 R^{27}, a bond to the linking group or a bond to the surfactant;

or alternatively,

R^9 and R^{10} are taken together with the carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-1 heteroatoms selected from O, N, , said ring system optionally substituted with a bond to the linking group or a bond to the surfactant; and

R^{12} is independently C_{1-6} alkyl;

R^{27} is =O, C1-4 alkyl, or phenyl substituted with R^{28};

R^{28} is a phenoxy group substituted with 0-2 OCH_3 groups;

R^{29} and R^{30} taken together with the nitrogen atom through which they are attached form a C5-7 atom saturated ring system substituted with R^{31}; and

R^{31} is a benzyloxy group substituted with C1-4 alkyl.

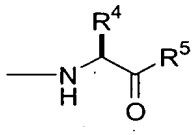
57. A diagnostic agent according to claim 55 wherein the targeting moiety is a matrix metalloproteinase inhibitor of the formulae (Ia) or (Ib):

wherein:

R is -OH;

R^2 is C_{1-6} alkyl;

X is C=O;

R^3 is  ;

R^1 and R^4 are taken together to form a bridging group of formula $-(CH_2)_3$-O-phenyl-CH_2-;

R^5 is NH(C1-6alkyl), substituted with a bond to the linking group or a bond to the surfactant.

58. A diagnostic agent according to claim 55 wherein:

R is -OH;

R^9 is C_1 alkyl substituted with a bond to Ln;

R^{10} and R^{11} taken together with the nitrogen atom to which they are attached form a 5 atom saturated ring system, said right system is substituted with 0-3 R^{27};

R^{27} is =O, C1-4 alkyl, or phenyl substituted with R^{28}; and

R^{28} is a phenoxy group substituted with 0-2 OCH_3 groups.

59. A diagnostic agent according to claim 55 wherein the

R is -OH;

R^1 and R^2 taken together with the nitrogen and carbon atom through which they are attached form a C_{5-7} atom saturated ring system substituted with one or more substituents selected from

the group consisting of: a bond to Ln, a bond to Sf, and $-C(=O)-NR^{29}R^{30}$;

R^{29} and R^{30} taken together with the nitrogen atom through which they are attached form a C5-7 atom saturated ring system substituted with R^{31}; and

R^{31} is a benzyloxy group substituted with C1-4 alkyl.

60. A diagnostic agent according to claim 48 wherein the linking group is of the formula:

$((W^1)_h-(CR^{13}R^{14})_g)_x-(Z)_k-((CR^{13a}R^{14a})_{g'}-(W^2)_{h'})_{x'}$;

W^1 and W^2 are independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, $NR^{15}C(=O)$, $C(=O)NR^{15}$, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO_2, SO_2NH, $-(OCH_2CH_2)_{76-84}$, $(OCH_2CH_2)_s$, $(CH_2CH_2O)_{s'}$, $(OCH_2CH_2CH_2)_{s''}$, $(CH_2CH_2CH_2O)_t$, and $(aa)_{t'}$;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R^{16}, C_{3-10} cycloalkyl substituted with 0-3 R^{16}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{16};

R^{13}, R^{13a}, R^{14}, R^{14a}, and R^{15} are independently selected at each occurrence from the group: H, =O, COOH, SO_3H, PO_3H, C_1-C_5 alkyl substituted with 0-3 R^{16}, aryl substituted with 0-3 R^{16}, benzyl substituted with 0-3 R^{16}, and C_1-C_5 alkoxy substituted with 0-3 R^{16}, $NHC(=O)R^{17}$, $C(=O)NHR^{17}$, $NHC(=O)NHR^{17}$, NHR^{17}, R^{17}, and a bond to the surfactant;

R^{16} is independently selected at each occurrence from the group: a bond to the surfactant, $COOR^{17}$, $C(=O)NHR^{17}$, $NHC(=O)R^{17}$, OH, NHR^{17}, SO_3H, PO_3H, $-OPO_3H_2$, $-OSO_3H$, aryl substituted with 0-3 R^{17}, C_{1-5} alkyl substituted with 0-1 R^{18}, C_{1-5} alkoxy substituted with 0-1 R^{18}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{17};

R^{17} is independently selected at each occurrence from the group: H, alkyl substituted with 0-1 R^{18}, aryl substituted with 0-1 R^{18}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{18}, C_{3-10} cycloalkyl substituted with 0-1 R^{18}, polyalkylene glycol substituted with 0-1 R^{18}, carbohydrate substituted with 0-1 R^{18}, cyclodextrin substituted with 0-1 R^{18}, amino acid substituted with 0-1 R^{18}, polycarboxyalkyl substituted with 0-1 R^{18}, polyazaalkyl substituted with 0-1 R^{18}, peptide substituted with 0-1 R^{18}, wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to the surfactant;

R^{18} is a bond to the surfactant;

k is selected from 0, 1, and 2;
h is selected from 0, 1, and 2;
h' is selected from 0, 1, and 2;
g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s" is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

t is selected from 0, 1, 2, 3, 4, 5; 6, 7, 8, 9, and 10;
t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
x is selected from 0, 1, 2, 3, 4, and 5; and
x' is selected from 0, 1, 2, 3, 4, and 5.

61. A diagnostic agent according to claim 60 wherein W^1 and W^2 are independently selected at each occurrence from the group: O, NH, NHC(=O), C(=O)NH, $NR^{15}C(=O)$, $C(=O)NR^{15}$, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO_2, $-(CH_2CH_2O)_{76-84}-$, $(OCH_2CH_2)_s$, $(CH_2CH_2O)_{s'}$, $(OCH_2CH_2CH_2)_{s''}$, $(CH_2CH_2CH_2O)_t$, and $(aa)_{t'}$;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-1 R^{16}, C_{3-10} cycloalkyl substituted with 0-1 R^{16}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{16};

R^{13}, R^{13a}, R^{14}, R^{14a}, and R^{15} are independently selected at each occurrence from the group: H, =O, COOH, SO_3H, C_1-C_5 alkyl substituted with 0-1 R^{16}, aryl substituted with 0-1 R^{16}, benzyl substituted with 0-1 R^{16}, and C_1-C_5 alkoxy substituted with 0-1 R^{16}, $NHC(=O)R^{17}$, $C(=O)NHR^{17}$, $NHC(=O)NHR^{17}$, NHR^{17}, R^{17}, and a bond to the surfactant;

k is 0 or 1;
s is selected from 0, 1, 2, 3, 4, and 5;
s' is selected from 0, 1, 2, 3, 4, and 5;
s" is selected from 0, 1, 2, 3, 4, and 5; and
t is selected from 0, 1, 2, 3, 4, and 5.

62. A diagnostic agent according to claim 60

wherein:

W^1 is $C(=O)NR^{15}$;

h is 1;

g is 3;

R^{13} and R^{14} are independently H;

x is 1;

k is 0;

g'is 0;

h' is 1;

W^2 is NH; and

x' is 1.

63. A diagnostic agent according to claim 60

x is 0;

k is 1;

Z is aryl substituted with 0-3 R^{16};

g' is 1;

W^2 is NH;

R^{13a} and R^{14a} are independently H;

h' is 1; and

x' is 1.

64. A diagnostic agent according to claim 60

W^1 is $C(=O)NR^{15}$;

h is 1;

g is 2;

R^{13} and R^{14} are independently H;

x is 1;

k is 0;

g' is 1;

R^{13a} and R^{14a} are independently H; or C1-5 alkyl substituted with 0-3 R^{16};

R^{16} is SO_3H;

W^2 is NHC(=O) or NH;

h' is 1; and
x' is 2.

65. A diagnostic agent according to claim 60
W^1 is C(=O)NH;
h is 1;
g is 3;
R^{13} and R^{14} are independently H;
k is 0;
g' is 0;
x is 1;
W^2 is -NH(C=O)- or $-(OCH_2CH_2)_{76-84}-$;
h' is 2; and
x' is 1.

66. A diagnostic agent according to claim 60
x is 0;
k is 0;
g' is 3;
h' is 1;
W^2 is NH; and
x' is 1.

67. A diagnostic agent according to claim 60
x is 0;
Z is aryl substituted with 0-3 R^{16};
k is 1;
g' is 1;
$R^{13a}R^{14a}$ are independently H;
W^2 is NHC(=O) or $-(OCH2CH2)_{76-84}-$; and
x' is 1.

68. A diagnostic agent according to claim 60
W^1 is C=O;
g is 2;

R^{13} and R^{14} are independently H;

k is 0;

g'is 0;

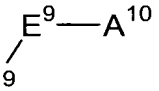
h' is 1;

W^2 is NH; and

x' is 1.

69. A diagnostic agent according to claim 48 wherein the linking group is present.

70. A diagnostic agent according to claim 48 wherein

S_f is a surfactant which is a lipid or a compound of the formula:  ;

A^9 is selected from the group: OH and OR^{32};

A^{10} is OR^{32};

R^{32} is $C(=O)C_{1-20}$ alkyl;

E^9 is C_{1-10} alkylene substituted with 1-3 R^{33};

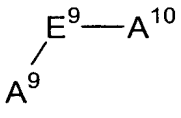
R^{33} is independently selected at each occurrence from the group: R^{35}, $-PO_3H-R^{35}$, =O, $-CO_2R^{34}$, $-C(=O)R^{34}$, $-C(=O)N(R^{34})_2$, $-CH_2OR^{34}$, $-OR^{34}$, $-N(R^{34})_2$, C_1-C_5 alkyl, and C_2-C_4 alkenyl;

R^{34} is independently selected at each occurrence from the group: R^{35}, H, C_1-C_6 alkyl, phenyl, benzyl, and trifluoromethyl;

R^{35} is a bond to L_n;

and a pharmaceutically acceptable salt thereof.

71. A diagnostic agent according to claim 48 wherein the surfactant is a lipid or a compound of the

formula:  ;

A^9 is OR^{32};

A^{10} is OR^{32};

R^{32} is $C(=O)C_{1-15}$ alkyl;

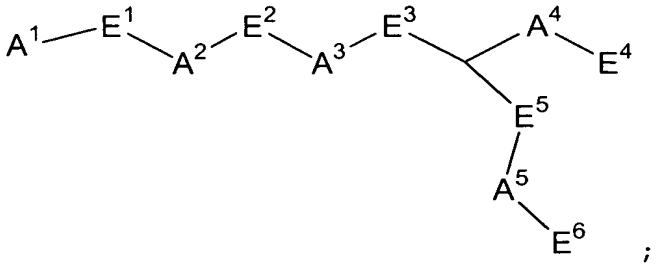
E^9 is C_{1-4} alkylene substituted with 1-3 R^{33};

R^{33} is independently selected at each occurrence from the group: R^{35}, $-PO_3H-R^{35}$, =O, $-CO_2R^{34}$, $-C(=O)R^{34}$, $-CH_2OR^{34}$, $-OR^{34}$, and C_1-C_5 alkyl;

R^{34} is independently selected at each occurrence from the group: R^{35}, H, C_1-C_6 alkyl, phenyl, and benzyl; and

R^{35} is a bond to L_n.

72. A diagnostic agent according to claim 48, wherein



;

wherein:

A^1 ia a bond to Ln;

E^1 is C_1 alkyl substituted by R^{23};

A^2 is NH;

E^2 is C_2 alkyl sunsttuted wth 0-1R^{23};

A^3 is -O-P(O)(R^{21})-O;

E^3 is C_1 alkyl;

A^4 and A^5 are each -O-;

E^4 and E^6 are each independently C_{1-16} alkyl substituted with 0-1R^{23};

E^5 is C_1 alkyl;

A^5 is -O-;

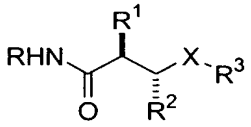
R^{21} is -OH; and

R^{23} is =O.

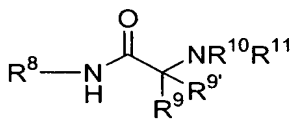
73. A diagnostic agent according to claim 48 wherein the compound is of the formula:

$$(Q)_d\text{-}L_n\text{-}S_f$$

wherein, Q is a compound of Formulae (Ia) or (Ib):



, or



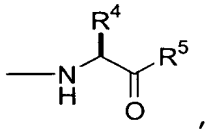
; wherein,

R is independently OH or $-CH_2SH$;

R^1 is independently selected at each occurrence from the group: H, OH, C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, and heterocycle-S-CH_2-;

R^2 is independently C_{1-20} alkyl;

X is independently C=O or SO_2, provided when X is C=O, R^3 is



, and when X is SO_2, R^3 is independently selected from the group: aryl substituted with 0-2 R^6, and heterocycle substituted with 0-2 R^6;

R^4 is independently selected at each occurrence from the group: C_{1-6} alkyl, phenyl, and benzyl;

R^5 is independently at each occurrence from the group: NH(C_{1-6} alkyl), NH-phenyl, and NH-heterocycle; wherein said alkyl, phenyl and heterocycle groups are optionally substituted with a bond to L_n;

R^6 is independently aryloxy substituted with 0-3 R^7;

R^7 is independently halogen or methoxy;

or alternatively,

R^1 and R^4 may be taken together to form a bridging group of the formula -$(CH_2)_3$-O-phenyl-CH_2-, optionally substituted with a bond to L_n;

or alternatively,

R^1 and R^2 may be taken together to form a bridging group of the formula $-(CH_2)_3-NH-$, optionally substituted with a bond to L_n; or

R^1 and R^2 taken together with the nitrogen and carbon atom through which they are attached form a C_{5-7} atom saturated ring system substituted with one or more substituents selected from the group consisting of: a bond to Ln, a bond to Sf, and $-C(=O)-NR^{29}R^{30}$;

R^8 is independently at each occurrence OH or phenyl, optionally substituted with a bond to L_n, provided that when R^8 is phenyl, R^{10} is $-C(=O)-CR^{12}-NH-CH(CH_3)-COOH$;

R^9 and $R^{9'}$ are independently H, C_{1-6} alkyl optionally substituted with a bond to L_n, or are taken together with the carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system substituted with R^6 and optionally substituted with a bond to L_n;

R^{10} and R^{11} are independently H, or C_{1-6} alkyl optionally substituted with a bond to L_n, or are taken together with the nitrogen atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted with 0-3 R^{27} or a bond to L_n;

or alternatively,

R^9 and R^{10} are taken together with the carbon atom to which they are attached to form a 5-7 atom saturated, partially

unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted with a bond to L_n;

R^{12} is independently C_{1-20} alkyl;

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

L_n is a linking group having the formula:

$((W^1)_h\text{-}(CR^{13}R^{14})_g)_x\text{-}(Z)_k\text{-}((CR^{13a}R^{14a})_{g'}\text{-}(W^2)_{h'})_{x'}$;

W^1 and W^2 are independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, $NR^{15}C(=O)$, $C(=O)NR^{15}$, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO_2, SO_2NH, $-(OCH_2CH_2)_{76-84}$, $(OCH_2CH_2)_s$, $(CH_2CH_2O)_{s'}$, $(OCH_2CH_2CH_2)_{s''}$, $(CH_2CH_2CH_2O)_t$, and $(aa)_{t'}$;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R^{16}, C_{3-10} cycloalkyl substituted with 0-3 R^{16}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{16};

R^{13}, R^{13a}, R^{14}, R^{14a}, and R^{15} are independently selected at each occurrence from the group: H, =O, COOH, SO_3H, PO_3H, C_1-C_5 alkyl substituted with 0-3 R^{16}, aryl substituted with 0-3 R^{16}, benzyl substituted with 0-3 R^{16}, and C_1-C_5 alkoxy substituted with 0-3 R^{16}, NHC(=O)R^{17}, C(=O)NHR^{17}, NHC(=O)NHR^{17}, NHR^{17}, R^{17}, and a bond to Sf;

R^{16} is independently selected at each occurrence from the group: a bond to Sf, $COOR^{17}$, $C(=O)NHR^{17}$, $NHC(=O)R^{17}$, OH, NHR^{17}, SO_3H, PO_3H, $-OPO_3H_2$, $-OSO_3H$, aryl substituted with 0-3 R^{17}, C_{1-5} alkyl substituted with 0-1 R^{18}, C_{1-5} alkoxy substituted with 0-1 R^{18}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{17};

R^{17} is independently selected at each occurrence from the group: H, alkyl substituted with 0-1 R^{18}, aryl substituted with 0-1 R^{18}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{18}, C_{3-10} cycloalkyl substituted with 0-1 R^{18}, polyalkylene glycol substituted with 0-1 R^{18}, carbohydrate substituted with 0-1 R^{18}, cyclodextrin substituted with 0-1 R^{18}, amino acid substituted with 0-1 R^{18}, polycarboxyalkyl substituted with 0-1 R^{18}, polyazaalkyl substituted with 0-1 R^{18}, peptide substituted with 0-1 R^{18}, wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to Sf;

R^{18} is a bond to Sf;

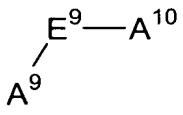
k is selected from 0, 1, and 2;
h is selected from 0, 1, and 2;
h' is selected from 0, 1, and 2;
g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s" is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

x is selected from 0, 1, 2, 3, 4, and 5;

x' is selected from 0, 1, 2, 3, 4, and 5;

S_f is a surfactant which is a lipid or a compound of the formula:



A^9 is selected from the group: OH and OR^{32};

A^{10} is OR^{32};

R^{32} is $C(=O)C_{1-20}$ alkyl;

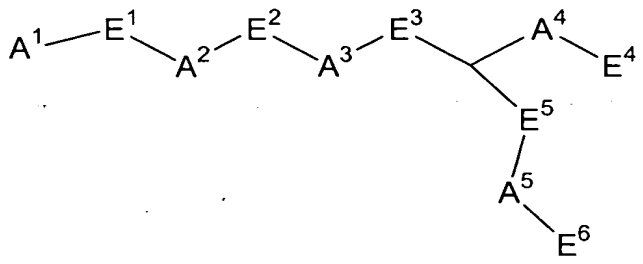
E^9 is C_{1-10} alkylene substituted with 1-3 R^{33};

R^{33} is independently selected at each occurrence from the group: R^{35}, $-PO_3H-R^{35}$, =O, $-CO_2R^{34}$, $-C(=O)R^{34}$, $-C(=O)N(R^{34})_2$, $-CH_2OR^{34}$, $-OR^{34}$, $-N(R^{34})_2$, C_1-C_5 alkyl, and C_2-C_4 alkenyl;

R^{34} is independently selected at each occurrence from the group: R^{35}, H, C_1-C_6 alkyl, phenyl, benzyl, and trifluoromethyl;

R^{35} is a bond to L_n; or

Sf is of the formula:



;

wherein:

A^1 ia a bond to Ln;

E^1 is C_1 alkyl substituted by R^{23};

A^2 is NH;

E^2 is C_2 alkyl sunsttuted wth 0-1R^{23};

A^3 is -O-P(O)(R^{21})-O;

E^3 is C_1 alkyl;

A^4 and A^5 are each -O-;

E^4 and E^6 are each independently C_{1-16} alkyl substituted with 0-1R^{23};

E^5 is C_1 alkyl;

A^5 is -O-;

R^{21} is -OH; and

R^{23} is =O; or

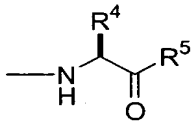
a pharmaceutically acceptable salt thereof.

74. A diagnostic agent according to Claim 73, wherein:

R is -OH;

R^2 is C1—6 alkyl;

X is C=O;

R^3 is  ;

R^1 and R^4 are taken together to form a bridging group of formula $-(CH_2)_3$-O-phenyl-CH_2-;

R^5 is NH(C1-6alkyl), substituted with a bond to the linking group or a bond to the surfactant.

75. A diagnostic agent according to Claim 73, wherein:

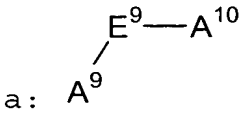
R is -OH;

R^9 is C_1 alkyl substituted with a bond to Ln;

R^{10} and R^{11} taken together with the nitrogen atom to which they are attached form a 5 atom saturated ring system, said right system is substituted with 0-3 R^{27};

R^{27} is =O, C1-4 alkyl, or phenyl substituted with R^{28}; and

R^{28} is a phenoxy group substituted with 0-2 OCH_3 groups;

S_f is a surfactant which is a lipid or a compound of the formula:  ;

A^9 is OR^{32};

A^{10} is OR^{32};

R^{32} is $C(=O)C_{1-15}$ alkyl;

E^9 is C_{1-4} alkylene substituted with 1-3 R^{33};

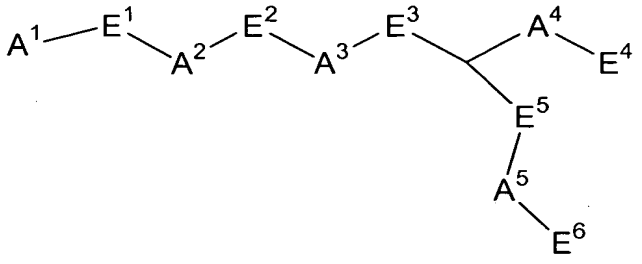
R^{33} is independently selected at each occurrence from the group: R^{35}, $-PO_3H-R^{35}$, =O, $-CO_2R^{34}$, $-C(=O)R^{34}$, $-CH_2OR^{34}$, $-OR^{34}$, and C_1-C_5 alkyl;

R^{34} is independently selected at each occurrence from the group: R^{35}, H, C_1-C_6 alkyl, phenyl, and benzyl; and

R^{35} is a bond to L_n.

76. A diagnostic agent according to Claim 73, wherein:
R is -OH;
R^9 is C_1 alkyl substituted with a bond to Ln;
R^{10} and R^{11} taken together with the nitrogen atom to which they are attached form a 5 atom saturated ring system, said right system is substituted with 0-3 R^{27};
R^{27} is =O, C1-4 alkyl, or phenyl substituted with R^{28}; and
R^{28} is a phenoxy group substituted with 0-2 OCH_3 groups;

S_f is a surfactant which is a lipid or a compound of the of the formula:



;

wherein:

A^1 ia a bond to Ln;

E^1 is C_1 alkyl substituted by R^{23};

A^2 is NH;

E^2 is C_2 alkyl sunsttuted wth 0-1R^{23};

A^3 is -O-P(O)(R^{21})-O;

E^3 is C_1 alkyl;

A^4 and A^5 are each -O-;

E^4 and E^6 are each independently C_{1-16} alkyl substituted with 0-1R^{23};

E^5 is C_1 alkyl;

A^5 is -O-;

R^{21} is -OH; and

R^{23} is =O.

77. A diagnostic agent according to Claim 73, wherein: wherein

R is -OH;

R^1 and R^2 taken together with the nitrogen and carbon atom through which they are attached form a C_{5-7} atom saturated ring system substituted with one or more substituents selected from the group consisting of: a bond to Ln, a bond to Sf, and -C(=O)-$NR^{29}R^{30}$;

R^{29} and R^{30} taken together with the nitrogen atom through which they are attached form a C5-7 atom saturated ring system substituted with R^{31}; and

R^{31} is a benzyloxy group substituted with C1-4 alkyl.

d is selected from 1, 2, 3, 4, and 5;

W is independently selected at each occurrence from the group: O, NH, NHC(=O), C(=O)NH, $NR^{15}C(=O)$, $C(=O)NR^{15}$, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO_2, $(OCH_2CH_2)_s$, $(CH_2CH_2O)_{s'}$, $(OCH_2CH_2CH_2)_{s''}$, $(CH_2CH_2CH_2O)_t$, and $(aa)_{t'}$;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-1 R^{16}, C_{3-10} cycloalkyl substituted with 0-1 R^{16}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{16};

R^{13}, R^{13a}, R^{14}, R^{14a}, and R^{15} are independently selected at each occurrence from the group: H, =O, COOH, SO_3H, C_1-C_5 alkyl substituted with 0-1 R^{16}, aryl substituted with 0-1 R^{16}, benzyl substituted with 0-1 R^{16}, and C_1-C_5 alkoxy substituted with 0-1 R^{16}, $NHC(=O)R^{17}$, $C(=O)NHR^{17}$, $NHC(=O)NHR^{17}$, NHR^{17}, R^{17}, and a bond to Sf;

k is 0 or 1;
s is selected from 0, 1, 2, 3, 4, and 5;
s' is selected from 0, 1, 2, 3, 4, and 5;
s" is selected from 0, 1, 2, 3, 4, and 5; and
t is selected from 0, 1, 2, 3, 4, and 5.

78. A diagnostic agent according to Claim 73, wherein:
W^1 is $C(=O)NR^{15}$;
h is 1;

g is 3;

R^{13} and R^{14} are independently H;

x is 1;

k is 0;

g'is 0;

h' is 1;

W^2 is NH; and

x' is 1.

79. A diagnostic agent according to Claim 73, wherein:

x is 0;

k is 1;

Z is aryl substituted with 0-3 R^{16};

g' is 1;

W^2 is NH;

R^{13a} and R^{14a} are independently H;

h' is 1; and

x' is 1.

80. A diagnostic agent according to Claim 73, wherein:

W^1 is $C(=O)NR^{15}$;

h is 1;

g is 2;

R^{13} and R^{14} are independently H;

x is 1;

k is 0;

g' is 1;

R^{13a} and R^{14a} are independently H; or C1-5 alkyl substituted with 0-3 R^{16};

R^{16} is SO_3H;

W^2 is NHC(=O) or NH;

h' is 1; and

x' is 2.

81. A diagnostic agent according to Claim 73, wherein:

W^1 is C(=O)NH;

h is 1;

g is 3;

R^{13} and R^{14} are independently H;

k is 0;

g' is 0;

x is 1;

W^2 is -NH(C=O)- or $-(OCH_2CH_2)_{76-84}-$;

h' is 2; and

x' is 1.

82. A diagnostic agent according to Claim 73, wherein:

x is 0;

k is 0;

g' is 3;

h' is 1;

W^2 is NH; and

x' is 1.

83. A diagnostic agent according to Claim 73, wherein:

x is 0;

Z is aryl substituted with 0-3 R^{16};

k is 1;

g' is 1;

$R^{13a}R^{14a}$ are independently H;

W^2 is NHC(=O) or $-(OCH2CH2)_{76-84}-$; and

x' is 1.

84. A diagnostic agent according to Claim 73, wherein:

W^1 is C=O;

g is 2;

R^{13} and R^{14} are independently H;

k is 0;

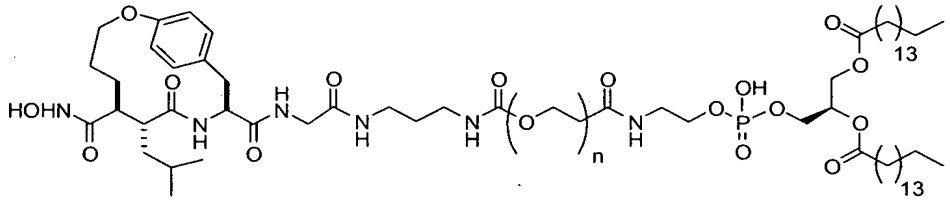
g'is 0;

h' is 1;

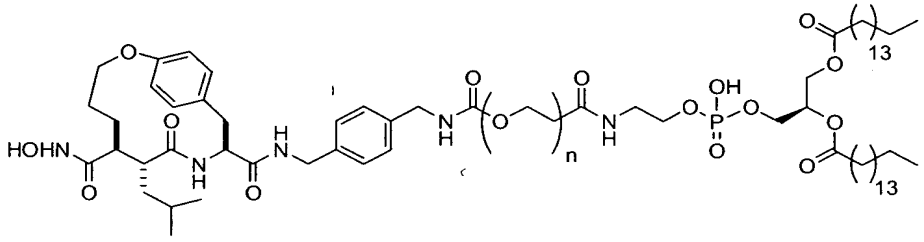
W^2 is NH; and

x' is 1.

85. A diagnostic agent according to Claim 1, wherein the compound is selected from the group consisting of:



; and



84. A diagnostic agent according to Claim 48, wherein:wherein the echogenic gas is a perfluorocarbon gas or sulfur hexafluoride.

87. A diagnostic agent according to claim 86 wherein said perfluorocarbon is selected from the group consisting of perfluoromethane, perfluoroethane, perfluoropropane, perfluorobutane, perfluorocyclobutane, perfluoropentane, and perfluorohexane.

88. A diagnostic composition comprising a compound according to claim 48 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

89. A diagnostic composition comprising a compound according to claim 48 or a pharmaceutically acceptable salt form

thereof, an echogenic gas and a pharmaceutically acceptable carrier.

90. A diagnostic composition comprising a compound according to claim 48 further comprising: 1,2-dipalmitoyl-sn-glycero-3-phosphotidic acid, 1,2-dipalmitoyl-sn-glycero-3-phosphatidylcholine, and N-(methoxypolyethylene glycol 5000 carbamoyl)-1,2-dipalmitoyl-sn-glycero-3-phosphatidylethanolamine.

91. A method of detecting, imaging or monitoring the presence of matrix metalloproteinase in a patient comprising the steps of:

a) administering to said patient a diagnostic agent of claim 1; and

b) acquiring an image of a site of concentration of said diagnostic agent in the patient by a diagnostic imaging technique.

92. A method of detecting, imaging or monitoring the presence of matrix metalloproteinase in a patient comprising the steps of:

a) administering to said patient a diagnostic agent of claim 48; and

c) acquiring an image of a site of concentration of said diagnostic agent in the patient by a diagnostic imaging technique.

93. A method of detecting, imaging or monitoring a pathological disorder associated with matrix metalloproteinase activity in a patient comprising the steps of:

a) administering to said patient a diagnostic agent of claim 1; and

b) acquiring an image of a site of concentration of said diagnostic agent in the patient by a diagnostic imaging technique.

94. A method of detecting, imaging or monitoring a pathological disorder associated with matrix metalloproteinase activity in a patient comprising the steps of:

a) administering to said patient a diagnostic agent according to claim 48; and

c) acquiring an image of a site of concentration of said diagnostic agent in the patient by a diagnostic imaging technique.

95. A method of detecting, imaging or monitoring atherosclerosis in a patient comprising the steps of:

a) administering a diagnostic agent according to claim 1; and

b) acquiring an image of a site of concentration of said diagnostic agent in the body by a diagnostic imaging technique.

96. A method of detecting, imaging or monitoring atherosclerosis in a patient comprising the steps of:

c) administering a diagnostic agent according to claim 48; and

d) acquiring an image of a site of concentration of said diagnostic agent in the body by a diagnostic imaging technique.

97. A method according to claim 95, wherein the atherosclerosis is coronory atherosclerosis or cerebrovascular atherosclerosis.

98. A method according to claim 96, wherein the atherosclerosis is coronory atherosclerosis or cerebrovascular atherosclerosis.

99. A method of identifying a patient at high risk for transient ischemic attacks or stroke by determining the degree of active atherosclerosis in a patient comprising carrying out the method of claim 96.

100. A method of identifying a patient at high risk for transient ischemic attacks or stroke by determining the degree of active atherosclerosis in a patient comprising carrying out the method of claim 97.

101. A method of identifying a patient at high risk for acute cardiac ischemia, myocardial infarction or cardiac death by determining the degree of active atherosclerosis by imaging the patient by the method of claim 96.

102. A method of identifying a patient at high risk for acute cardiac ischemia, myocardial infarction or cardiac death by determining the degree of active atherosclerosis by imaging the patient by the method of claim 97.

103. A method of simultaneous imaging of cardiac perfusion and extracellular matrix degradation in a patient comprising the steps of:

a) administering a diagnostic agent according to claim 1, wherein the diagnostic metal is a gamma-emitting radioisotope; and

(b) administering a cardiac perfusion compound, wherein the compound is radiolabeled with a gamma-emitting radioisotope which exhibits a gamma emission energy that is spectrally separable from the gamma emission energy of the diagnostic metal conjugated to the targeting moiety in step (a); and

(c) acquiring, by a diagnostic imaging technique, simultaneous images of the sites of concentration of the spectrally separable gamma-emission energies of the compounds administered in steps (a) and (b) .